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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/428,458	10/28/1999	KJETIL TASKEN	Q-56244	4681

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EXAMINER
SCHMIDT, MARY M

ART UNIT	PAPER NUMBER
1635	15

DATE MAILED: 09/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/428,458	Applicant(s) TASKEN ET AL.	
	Examiner Mary Schmidt	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Specification

1. The abstract of the disclosure is objected to because it is less that 50 words. Correction is required. See MPEP § 608.01(b).

2. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Claim Rejections - 35 USC § 112

3.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 45-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 45 is rejected for failure to recite a final step that relates back to the preamble to indicate that the claimed methods of treatment of an immunosuppressive disease have been achieved.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention

6. New claims 40-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of CVI, AIDS or HIV infection with the administration of Rp-8-Br-cAMPS, Rp-8-Cl-cAMPS and Rp-8-Br-monobutyryl-cAMPS (those compositions found to have function and lack of toxicity *in vivo*) for the inhibition of PKA type Iα, does not reasonably provide enablement for the breath of any cAMP antagonist for the functions claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for the same reasons of record set forth in the Official Action mailed 12/19/01.

Applicant's arguments filed 06/19/02 have been fully considered but they are not persuasive.

New claims 40-42 are drawn to pharmaceutical compositions for treating an immunosuppressive disease comprising (A) a pharmaceutically effective amount of a cAMP antagonist, wherein said cAMP antagonist is selected from the group consisting of Rp-8-Br-cAMPS, Rp-8-Br-monobutyryl-cAMPS, Rp-monobutyryl-cAMPS, Rp-8-(4-chlorophenyl-thio)-cAMPS and Rp-piperidino-cAMPS; and (B) a pharmaceutically acceptable adjuvant or filler; wherein the immunosuppressive disease is selected from the group consisting of AIDS, HIV injection and CVI.

New claims 43-50 are drawn to methods of administering to a subject a pharmaceutical compositions comprising any cAMP antagonist (claim 45) or specifically (A) a pharmaceutically effective amount of a cAMP antagonist, wherein said cAMP antagonist is selected from the group consisting of Rp-8-Br-cAMPS, Rp-8-Br-monobutyryl-cAMPS, Rp-monobutyryl-cAMPS, Rp-8-(4-chlorophenyl-thio)-cAMPS and Rp-piperidino-cAMPS (claim 43) or a thio-substituted cAMP analog, an equatorial diastereomer of 3'5'-cyclic adenosine monophosphorothioate (Rp-cAMPS) (claim 47) and (B) a pharmaceutically acceptable adjuvant or filler, so as to inhibit the localization of PKA type Iα isozyme with T cell receptor/CD3 complexes (claim 43); or selectively or specifically abolish the function of cAMP dependent protein kinase (PKA) type Iα isozyme ($Ri\alpha_2C_2$); or the thio-substituted cAMP analog binds to an RIα subunit of said isozyme

and acts as a selective or specific antagonist (claim 47); wherein the immunosuppressive disease is selected from the group consisting of AIDS, HIV infection and CVI.

The Declaration by Kjetil Tasken, provides date collected from experiments where Rp-8Br-cAMPS and 8-Br-cAMP were administered to murine acquired immunodeficiency syndrome (MAIDS) mice. Section 8 of the declaration states that upon administration of 30 mg/kg/day of Rp-8-Br-cAMPs, no toxic effect of the compound was observed. Section 11 states that the T-cell immune function was assessed in crude lymph node cells from treated and control (PBS)-treated infected mice after 2 weeks of treatment and a 3-fold increase in Rp-8-Br-cAMPs over PBS cells as indicated by anti-CD3 detection. In section 13 of the declaration, Applicant's state that Table 2 shows reverse inhibition of T cell activation is also observed using other compounds (Rp-8-Cl-cAMPS and Rp-8-Br-monobutyryl-cAMPS).

Applicant's publication, Aukrust et al., "Increased Activation of Protein Kinase A Type I Contributes to the T Cell Deficiency in Common Variable Immunodeficiency", Journal of Immunology, 1999, 162: 1178-1185, further provides evidence that the administration of Rp-8-bromo-cAMP-phophorothioate markedly improved anti-CD3-stimulated proliferation in CVI patients. This reference further provides evidence as to the lack of toxicity. The Rp-8-bromo-cAMP-phosphorothioate *in vivo*.

Another post filing reference, Carlson et al. (Neoplasia, Sep-Oct, 2000, 2 (5), p441-8, abstract only considered and provided) states in the abstract that "[t]he cAMP analog 8-Cl-cAMP

induces apoptosis and inhibits proliferation of a wide variety of malignancies *in vitro* and *in vivo* with relatively little toxicity."

Although evidence of success of a potential therapeutic compound in compromised mice is not necessarily considered to correlate to success in other subjects such as human, Applicant's own data (J. Of Immunology) show that the administration of the Rp-8-bromo-cAMP-phosphorothioate is able to function in human. However, the successes argued by Applicant and the teachings of the post-art, do not provide an equivalent expectation of success for any cAMP antagonist, or the for the other specific antagonists claimed, but not shown to have an effect in the methods of treatments claimed. Absent such a teaching, the breath of cAMP antagonists not shown to have *in vivo* treatment effects are rejected for the same reasons of record as set forth in the previous Official Action because the amount of experimentation considered to make and use any such cAMP antagonist is considered undue based on the teachings of the instant specification as filed.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

8. Claims 40, 41 and 42 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 5,843,916.

The are drawn to compositions comprising a cAMP antagonist such as a thio-substituted cAMP analog, such as Rp-8-Br-cAMPS and Rp-8-Cl- cAMPS.

Applicant is reminded of the teachings of MPEP 2112.01which states that "[w]hen the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established." The compositions taught by U.S. Patent 5,843,916 have the same basic composition embraced by the instant claims and are thus anticipated by the prior art.

U.S. Patent '916 teaches throughout the specification, and especially in claims 18-24 pharmaceutical compositions comprising Rp-8-Br-cAMPS and Rp-8-Cl- cAMPS.

9. Claims 43-50 are considered free of the prior art since the prior art did not teach nor fairly suggest administration of the enabled Rp-8-Br-cAMPS, Rp-8-Cl-cAMPS and Rp-8-Br-monobutyryl-cAMPS *in vivo* for the inhibition of PKA type Iα and the treatment of AIDS, HIV infection or CVI as taught in the instant invention.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader*, may be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Analyst, *Kay Pinkney*, whose telephone number is (703) 305-3553.

SEAN McGARRY
PRIMARY EXAMINER
1635

M. M. Schmidt
September 9, 2002